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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/535,814	03/28/2000	Yuh-Jiuan Lin	64,600-024 CIP	5514

7590 05/11/2004

Tung & Associates
838 West Long Lake Road
suite 120
Bloomfield Hills, MI 48302

EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 05/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/535,814	LIN ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *04 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth on January 4, 2004, have been entered in full.

Response to Amendment

Applicant is notified that any outstanding objection or rejection that is not expressly maintained in this Office action has been withdrawn in view of Applicant's persuasive arguments and amendment to claim 1.

Priority

Issues of priority are now moot as the outstanding prior art rejections are withdrawn in view of Applicant's persuasive arguments.

Claim Objections

Claims 1 and 5 are objected to because of the following informalities: in line two of claim 1 the word "molecules" appears to be improperly in the plural, i.e. it appears that the word should be "molecule". Additionally the phrase "probably binding domains" as it appears in claims 1 and 5 is grammatically incorrect, i.e. the word "probable" should be used. Appropriate correction is required.

Specification

The amendment filed 1/2/04 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The specification has been

extensively altered, yet Applicant has not pointed out where in the original specification lies the support for each of these amendments. Applicant is required to either point-out where support can be found or cancel the new matter in the reply to this Office Action.

Sequence Rules Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons: the new amendment makes reference to specific polynucleotide and polypeptide sequences, e.g. at pages 9 and 10; these references must contain a sequence identifier of the form: SEQ ID NO: X. However, it should be pointed-out that these new sequence constitute new matter and need to be removed from the application. Appropriate correction is required.

Maintained Rejections:

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of making a biosensor comprising attaching the peptide DPDQRDC to a traducer, does not reasonably provide enablement for methods involving any other peptide and nor for the broadly claimed method of making a biosensor cable of detecting a molecule wherein the molecule is a ligand for an olfactory receptor. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification teaches that the peptide DPDQRDC binds trimethylamine with high affinity (e.g. Fig. 5). And that this peptide was discovered through a process of molecular modeling involving comparisons of a canine olfactory receptor protein with other known GPCRs and further computational methods to deduce possible ligand binding domains. This was followed by testing the various putative ligand binding peptides in an in vitro assay (pages 3-7). The specification, however, provides no specific details regarding the discovery of other ligand binding peptides and merely invites the skilled artisan to try to find them using the very generalized teaching in the specification. There appears to be no specific teaching as to how to find other peptides based on anything more than computational modeling followed by trial and error experimentation.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (see Bowie et al., 1990, Science 247:1306-1310, especially p.1306, column 2, paragraph 2; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure, pp 492-495, Birkhauser, Boston). However, Applicant has provided little or no guidance beyond the mere invitation to use available analytical programs to try and find other ligand binding peptides. Although the specification outlines art-recognized procedures for producing and screening for active proteins, this is not adequate guidance as to the nature of active proteins that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation.

Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore deletion of the remaining non-essential residues can often destroy activity.

As is appreciated in the art, the acquisition of structural information regarding receptors whether in the form of sequence data, three-dimensional crystallographic structures, or otherwise, requires extensive labor which is not of a routine nature in the study of integral membrane receptors - and the results of any experiment cannot be predicted merely because the receptor is at hand. The instant application sets forth a research plan, not an invention ready to be practiced. The teaching that an artisan could, for example, obtain a receptor sequence, make various prediction regarding its structure using various algorithms known in the art, and deduce the therefrom by unspecified means some possible sites of ligand interaction fails to teach the artisan how to actually practice the invention. "Tossing out the mere germ of an idea does not constitute enabling disclosure... [R]easonable detail must be provided in order to enable members of the public to understand and carry out the invention." Genentech, Inc. v. Novo Nordisk Inc., 108 F.3d 1361, 1366, 42 U.S.P.Q.2d 1001, 1005 (Fed. Cir. 1997). Such reasonable detail is lacking in the instant application. As was appreciated in the art, the development of any physical or conceptual model system requires considerable effort, creativity, insight, intuition and a good deal of experimentation. The instant application merely provides the skilled artisan with an invitation to gather such effort, creativity, insight,

intuition and good deal of experimentation, and, as such, does not meet the requirements of the first paragraph of 35 U.S.C. 112.

Additionally, the claims encompass methods that require that the biosensor utilize those ligands that endogenously activate the receptor. The specification has provided no guidance as to how to find such peptides. It is even unclear whether or not trimethylamine is a true ligand of the dog receptor used in example 1. The art recognizes the difficult problem of pairing ligands with olfactory receptors. In fact, Zhao et al. Science 279(237-242)1998 teach that although the odorant receptors may signal through a common motif, the putative odorant receptors constitute the largest subfamily of GPCRs, and in some ways remain the most enigmatic, because no particular mammalian receptor has been definitively paired with any ligand (see page 237, col 1).

Thus, due to the large quantity of experimentation necessary to generate the infinite number of peptides required by the claims and then to screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples other than the single disclosed peptide, the complex nature of the invention, the state of the prior art which establishes the unpredictability of matching ligands based on sequence data and modeled protein structure, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Applicant argues that the claims and the specification have been amended to supply sufficient detail so as to practice the invention. This argument has been fully considered but not deemed persuasive. The teachings in the specification are simply a

generalized research plan that simply invites the artisan to use computational modeling to try to find peptides that bind a ligand or ligands that bind a peptide. This clearly amounts to no more than an invitation to conduct basic research and cannot be the basis of a United States patent.

Applicant argues that the claim methods have been used by Applicants to produce peptides that bind ammonia, sulfur compounds and amine compounds. This argument has been fully considered but not deemed persuasive. While these peptides might form the basis of a patent, the call to try to find others cannot. Applicant argues that computational modeling produces a limited number of peptide compounds to be tested so the experiments are not random trial and error. This argument has been fully considered but not deemed persuasive. Nowhere in the specification is it taught how to choose which ligands should be modeled with which peptides, i.e. the choice necessarily involves the random trial and error decision to try to match either randomly chosen ligands with a particular peptide, or to try to randomly match peptides with a particular ligand. After, this, perhaps the decisions are narrowed by the results of the computational modeling, however an invitation to do this type of basic research is not patentable.

Applicant argues that the application does not intend to find the "true" tertiary structure of an active ORP or to find it's "true" ligand. This argument has been fully considered but not deemed persuasive. As set forth previously, whether intended or not, the claims encompass the acquisition of the true ligand and would be interpreted as such by one of ordinary skill in the art.

Conclusion

No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, Ph.D., can be reached at (571) 272-0887.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

MB

May 6, 2004